

IN THE SPECIFICATION

Please replace the paragraph beginning at page 59, line 5, with the following amended paragraph:

The residue was dissolved in dichloromethane (50 ml) and to this solution was added Compound [[b]] (5) (3.14 g), PyBOP® (4.86 g) and N,N-diisopropylethylamine (3.62 g) under ice-cooling, and the resulting mixture was stirred at ambient temperature for 16 hours. The volatiles were removed in vacuo and the residue was extracted with ethyl acetate (500 ml). The organic layer was washed with 5% aqueous potassium hydrogensulfate solution (200 ml, 4 times), saturated aqueous sodium bicarbonate solution (200 ml, twice), water (200ml, twice) and brine (100 ml). The residue was purified by flash chromatography (eluting with ethyl acetate/hexane = 2:1 v/v) to give Compound (16) (5.2 g) as a colorless amorphous solid.

Please replace the paragraph beginning at page 61, line 26 to page 62, line 2, with the following amended paragraph:

The Compound (21) (4.89 g) was dissolved in dichloromethane (40 ml) and Compound [[a]] (1) (4.31 g), benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (6.68 g) and N-ethyldiisopropylamine (4.83 g) were added to the solution, and the mixture was stirred for 15 hours at ambient temperature. The mixture was diluted with chloroform (40 ml), washed with 5% aqueous solution of potassium hydrogensulfate (50 ml), saturated aqueous sodium bicarbonate solution (50 ml) and saturated aqueous sodium chloride solution (50 ml), dried over sodium sulfate and evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 120 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (22) (5.70 g).

Please replace the paragraph beginning at page 67, line 26 to page 62, line 2, with the following amended paragraph:

Compound (41) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation [[C5]] 88.

Please replace the paragraph beginning at page 75, line 20, with the following amended paragraph:

A solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the Compound [[B1-1]] (65) (2.00 g) and the resulting suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered and then a solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the residual solid. The suspension was shaken for additional 15 minutes. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times). To the residual solid were added (S)-N-(9-fluorenylmethoxycarbonyl)phenylalanine (2.46 g), benzotriazole-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®; 3.31 g) and N,N-diisopropylethylamine (822 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 16 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times), dichloromethane (20 ml, 3 times) and isopropyl alcohol, and dried to give Compound (66) (2.08 g).

Please replace the paragraph beginning at page 77, line 27 to page 78, line 2, with the following amended paragraph:

The Compound (68) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 6 ml) for 1 hour. The suspension was filtered and the filtrate

was concentrated in vacuo to give Compound (69) (128 mg). The purity of the Compound [[B1-5]] (69) was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 40:60 rt=7.76 minutes. The Compound (69) was used in Preparation 103.

Please replace the paragraph beginning at page 160, line 4, with the following amended paragraph:

The Compound (342) was dissolved into a mixed solvent of methanol/dichloromethane (2/1, 60 ml), and the mixture was cooled in dry ice-acetone bath (internal temperature: about ~~70°C~~ -70°C) and bubbled with 1 to 2% of ozone in oxygen at the velocity of 1L/min for 15 min. The mixture was stirred under nitrogen atmosphere and then under oxygen atmosphere. To the mixture was added dimethyl sulfide (0.7 ml) and the mixture was stirred with raising the temperature to ambient temperature. The reaction mixture was evaporated and purified by flash column chromatography (Silica gel 60N, Spherical, 1108, eluting with ethyl acetate/hexane = 1/1, 3/2, then 2/1) and preparative thin layer chromatography (eluting with ethyl acetate/hexane = 1/1 then methanol/chloroform = 1/20) to give the objective Compound (343).

Please replace the paragraph beginning at page 219, line 27 to page 220, line 4, with the following amended paragraph:

To a stirred solution of dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate (812 mg) in water and tetrahydrofuran (1:40) (7.5 ml) was added barium hydroxide octahydrate (482 mg) in one portion. The mixture was stirred at ambient temperature for 30 minutes. To the mixture was added a solution of Compound [[C1-3]] (78) (980 mg) in water and tetrahydrofuran (1:40) (1.5 ml once, 1 ml twice), and stirred for 1

hour. 10% Aqueous citric acid solution (50 ml) was added to the mixture to quench the reaction, stirred for 15 minutes under ice-cooling, and extracted with ethyl acetate (300 ml). The organic layer was washed with 10% citric acid (50 ml), water (50 ml) and brine (50 ml), dried over sodium sulfate and evaporated in vacuo. The residue was purified by flash column chromatography (eluting with ethyl acetate/hexane = 2:3 to 1:1 v/v) to give Compound E1 as a white foam (852 mg).

Please replace the paragraph beginning at page 264, line 23 to page 265, line 1, with the following amended paragraph:

To a stirred solution of dimethyl 3-fluoro-2-oxopropylphosphonate (86.1 mg) in 2-propanol (3 ml) was added cesium carbonate (152 mg) at ambient temperature and the mixture was stirred at the same temperature for half an hour. To the resulting light yellow solution was added a solution of the starting compound (Compound (105)) (200 mg) in isopropyl alcohol at the same temperature and the mixture was stirred at the same temperature for two hours. The reaction mixture was quenched with 10% aqueous solution of citric acid, diluted with ethyl acetate and water. The organic layer was separated and washed with saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 66% ethyl acetate/hexane (v/v) as a solvent mixture to give Compound E144 (68 mg) as a white amorphous solid.